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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,586	10/17/2001	George A. Gaitanaris	50001/002005	7567
21559	7590	05/17/2006	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/982,586

Applicant(s)

GAITANARIS, GEORGE A.

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-13,18 and 20-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-13,18 and 20-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1, 2, 6-13, 18, 20-24 are pending in the application.

This Office Action is in response to the amendment filed on 2/10/06.

Response to Amendment

The rejection of claims 1, 2, 6-13, 18, 20-24 under 35 U.S.C. 103 (a) is maintained for reasons set forth of the record mailed on 9/8/05 and further discussed below.

Response to Arguments

Claims 1, 2, 6-8, 20, 21, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furth et al (1994, PNAS, Vol.91, pages 9302-9306, IDS), in view of Friedrich et al (1991, Genes and Development, Vol. 5, pages 1513-1523).

In response to this rejection, Applicants argue that the cited art does not provide a motivation to combine the teaching and reach the claimed invention. Applicants assert that the teaching of Furth is similar to the previously cited but now withdrawn reference by St. Onge, wherein the reporter gene is regulated by tetracycline withdraw, which suffers from the same deficiency as St. Onge. Applicants further assert that Friedrich is solely focused on the development of a method for more easily selecting insertion mutations in mice, and is silent on the use of a regulatory gene. Applicants also indicate two distinctions between the mice of Furth and the claimed mouse, first being ubiquitously gene expression by Furth, wherein the claimed invention expresses the gene in a spatial restricted manner, second being whether an endogenous gene is mutagenized. Applicants thus conclude that neither reference provides motivation to combine the reference and reach the claimed invention. Moreover, Applicants argue that the combined teaching would not result in the claimed invention, but a mouse with three transgenes.

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Applicants also argue that the combine reference does not teach or suggest the inclusion of a transcription terminator as claimed. Applicants assert that there is special advantage for including such a sequence such as preventing read through transcription of flanking cellular sequences and increasing the mutagenic capability. Applicants thus conclude that claimed invention is not obvious in view of cited references.

Applicant's argument has been fully considered but deemed unpersuasive. The reason for the obviousness of the claimed invention was discussed in detail in the office action mailed on 9/8/05. In response to Applicant's argument with regard to the similarity between Furth and St. Onge, it is noted that similar teaching with a previously cited reference does not necessary mean Furth et al. has the same deficiency. Applicants fail to explain why the regulation of the reporter expression by tetracycline would constitute a deficiency. The claim recites a second transgene which integrates into the genome of the mouse that is capable of being regulated by the first transgene which encodes a regulatory protein, such recitation does not exclude the presence or absence of additional regulatory factor, such as tetracycline. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant's characterization of Friedrich reference is problematic because Applicants have focused on the rapid screening aspects of the transgenic mouse, but ignored why such mouse are being generated, namely to study gene activity during development and the function of the promoter. With regard to the arguments directed to Furth et al., Applicants are reminded that the instant claim does not require the transgene are expressed in a

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spatial restricted manner, the only requirement is the first transgene encodes a regulatory protein that regulates the expression of a second transgene regardless of the nature of said transgene (whether being reporter or not). Moreover, the transgene taught by Furth does mutagenizes endogenous gene because the insertion of the foreign DNA into an endogenous loci of the genome would consider to be mutation to said endogenous gene (Applicants are reminded that endogenous gene includes not only exon but intron as well). Even if this reference fails to mention any endogenous gene being mutated, this element is clearly taught by Friedrich et al. Applicants are reminded that this is not a 102 rejection, wherein a single reference must anticipates every element of the claimed invention. Furthermore, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation is clearly set forth in both articles, of which not only to study the function of the mutated gene (as taught by Friedrich), but also provides a spatial and temporal gene regulatory system as taught by Furth (see page 9306, last paragraph) that utilizes the advantage of tissue specific expression of an endogenous gene. Applicants fail to explain why this is not a motivation to combine the references.

Moreover, Applicants fail to explain why the combined teaching of Furth and Friedrich would result in a mouse with three transgene. The fact that applicant has recognized another

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advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Lastly, at the time of filing, using an transcription terminator is routine in the art of making vectors that expresses heterologous protein in either prokaryotic or eukaryotic cells. Although Furth and Friedrich do not specifically mention the inclusion of a transcription terminator, it would have been obvious to one of ordinary skill in the art would have include a transcription terminator at the end of a transgene for prevent transcriptional read through. Inclusion of the transcription terminator at the end of the transgene is not a novel aspect of the claimed invention. Therefore, for reasons set forth of the record and discussed above, the claimed invention is obvious in view of cited art.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furth et al., in view of Friedrich et al., as applied to claims 1, 2, 6-8, 20, 21, 23 and 24 above, and further in view of Zhang et al (1996, BBRC, vol.227, pages 707-711).

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Furth et al. and Friedrich et al., as applied to claims 1, 2, 6-8, 20, 21, 23 and 24 above, and further in view of Bremer et al.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Furth et al. and Friedrich et al., as applied to claims 1, 2, 6-8, 20, 21, 23 and 24 above, and further in view of Smith et al. (US 6, 150,169)

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Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Furth et al. and Friedrich et al., as applied to claims 1, 2, 6-8, 20, 21, 23 and 24 above, and further in view of Borrelli et al. (1988, PNAS, Vol. 85, pages 7572-7576).

In response to this rejection, Applicants argue that none of the references cited, namely, Zhang et al., Bremmer et al., Smith et al., and Borrelli et al. remedies the deficiencies of Furth et al and Friedrich et al. by providing the transcription terminator or the motivation to make the claimed mouse. Applicants thus conclude that claimed invention is not obvious in view of cited references.

Applicants' argument have been fully considered but deemed unpersuasive. The combined teaching of Furth and Friedrich renders claims 1, 2, 6-8, 20, 21, 23 and 24 obvious for reasons discussed above. Zhang et al., Bremmer et al., Smith et al., and Borrelli et al. remedies the deficiencies of Furth et al and Friedrich et al. are cited to provide teaching with regard to specific elements recited in claims 9-13, 18 and 22. Since Applicants provide no additional reasoning why these references are deficient, the rejection is maintained for same reason set forth of the record mailed on 9/8/05 and discussed above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER

